Annual Surveillance Summary: *Clostridium difficile* Infections in the Military Health System (MHS), 2016

NMCPHC-EDC-TR-364-2017

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14. ABSTRACT
The EpiData Center Department (EDC) conducts routine surveillance of Clostridium difficile (CD) incidence among all beneficiaries seeking care within the Military Health System (MHS). This report is a calendar year (CY) 2016 update to the CY 2015 annual report on C. difficile infection (CDI) among MHS beneficiaries. CDI incidence in the MHS population in both CY 2016 and CY 2015 showed normal variation when compared to the average annual incidence for CYs 2013-2015 and 2012-2014, respectively. Demographic and clinical characteristics in CY 2016 were similar to trends reported in CY 2015. The burden of CDI continues to largely manifest in the community setting, among beneficiaries aged 45 years and older, and in patients with previous antibiotic and gastric-acid suppressant use. Patients with CDI and specific comorbidities, such as diabetes, renal failure, chronic obstructive pulmonary disease (COPD), and cancers, represent a patient group within the MHS population that is especially vulnerable to worse health outcomes, such as recurrent CDI and increased risk of mortality. This group may especially benefit from prompt CDI identification and treatment. Interventions that reduce antibiotic exposure are the primary measures recommended to reduce CDI.

15. SUBJECT TERMS
Health Level 7 (HL7), microbiology, surveillance, Clostridium difficile, Military Health System (MHS), multi-drug resistance (MDR), hospital-associated infection (HAI), community-associated (CA) infection

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Abstract

The EpiData Center Department (EDC) conducts routine surveillance of *Clostridium difficile* (CD) incidence among all beneficiaries seeking care within the Military Health System (MHS). This report is a calendar year (CY) 2016 update to the CY 2015 annual report on *C. difficile* infection (CDI) among MHS beneficiaries.

Multiple data sources were linked to assess descriptive and clinical factors related to CD. Health Level 7 (HL7)-formatted microbiology and chemistry data identified CDI. These infections were matched to HL7-formatted pharmacy data to assess prescription practices and the Standard Inpatient Data Record (SIDR) to determine healthcare-associated exposures.

CDI incidence in the MHS population in both CY 2016 and CY 2015 showed normal variation when compared to the average annual incidence for CYs 2013-2015 and 2012-2014, respectively. Demographic and clinical characteristics in CY 2016 were similar to trends reported in CY 2015. The burden of CDI continues to largely manifest in the community setting, among beneficiaries aged 45 years and older, and in patients with previous antibiotic and gastric-acid suppressant use. Patients with CDI and specific comorbidities, such as diabetes, renal failure, chronic obstructive pulmonary disease (COPD), and cancers, represent a patient group within the MHS population that is especially vulnerable to worse health outcomes, such as recurrent CDI and increased risk of mortality. This group may especially benefit from prompt CDI identification and treatment.

Interventions that reduce antibiotic exposure are the primary measures recommended to reduce CDI incidence and recurrence. These measures include limiting the use of unnecessary antibiotics, prescribing antibiotics that are lower risk for contributing to CDI, and using antibiotics for the shortest reasonable duration. The MHS population can benefit from these interventions to decrease both CDI incidence and antibiotic selective pressure that may influence the development of multidrug-resistant organisms.

Contents

Background, Methods, and Limitations

The EpiData Center (EDC) at the Navy and Marine Corps Public Health Center (NMCPHC) prepares a retrospective report each calendar year (CY) that summarizes the demographics, clinical characteristics, and prescription practices for *C. difficile* infection (CDI) among Military Health System (MHS) beneficiaries.

Literature review did not provide any new developments or research for CDI. Additionally, no new methods or limitations were applied to this annual summary. As such, this report presents analytical results and discussion of CY 2016 data for CDI in the MHS. The methods and limitations relevant to this analysis have been discussed in a previous report (CY 2015 CDI annual report[1]).

The EDC also monitors other multidrug-resistant organisms (MDROs) of interest in the MHS.[2,3]

Results

Section A – Descriptive Epidemiology
Incidence of *Clostridium difficile*

In 2016, a total of 2,071 *Clostridium difficile* (CD) incident episodes occurred among 1,969 MHS beneficiaries treated at a military treatment facility (MTF). The overall annual CDI incidence rate (IR) was 22.0 per 100,000 persons per year, a 16.2% relative increase from the weighted historic average (Table 1). The 2016 rate was within two standard deviations (SDs) of the weighted average incidence rate. The Air Force, Army, and Navy rates also increased from the weighted historic IR but remained within two standard deviations of the weighted historic IR. However, the 2016 IR for the Marine Corps was 49.1% above the weighted historic IR and greater than two standard deviations above the historic observations.

Table 1. Incidence Rate (IR) for *C. difficile* Infections in the MHS, CY 2016

Population	2016 IR	Weighted Historic[a] IR 2013 - 2015	Two Standard Deviations: Weighted Historic[a] IR	2016	
				Direction	Percent Change
MHS	22.0	18.9	4.7	↑	16.2%
Air Force	21.4	19.1	4.9	↑	11.9%
Army	21.0	17.7	4.9	↑	18.5%
Marine Corps	19.7	13.2	5.5	↑	49.1%
Navy	18.9	16.6	4.2	↑	13.9%

Rates are presented as the rate per 100,000 persons per year.
A green arrow indicates an increasing percent change and a blue arrow indicates a decreasing percent change.
[a] Historic IR reflects the weighted average of the three years prior to the analysis year.
[b] This reflects the percent change from the weighted historic IR to the IR of the current analysis year.
Data Source: NMCPHC HL7-formatted CHCS microbiology, chemistry and MHS M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Regionally, the South, South Atlantic, West, and OCONUS incidence rates were approximately equal to or above the overall annual CDI MHS incidence rate, whereas the incidence rates in the Midwest and Northeast regions were lower than the overall annual rate (Figure 1).

Figure 1. Annual Incidence Rate (IR) for *C. difficile* Infections in the MHS by Region, CY 2016

Rates are presented as the rate per 100,000 persons per year.
Data Source: NMCPHC HL7-formatted CHCS microbiology, chemistry, SIDR, and MHS M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.
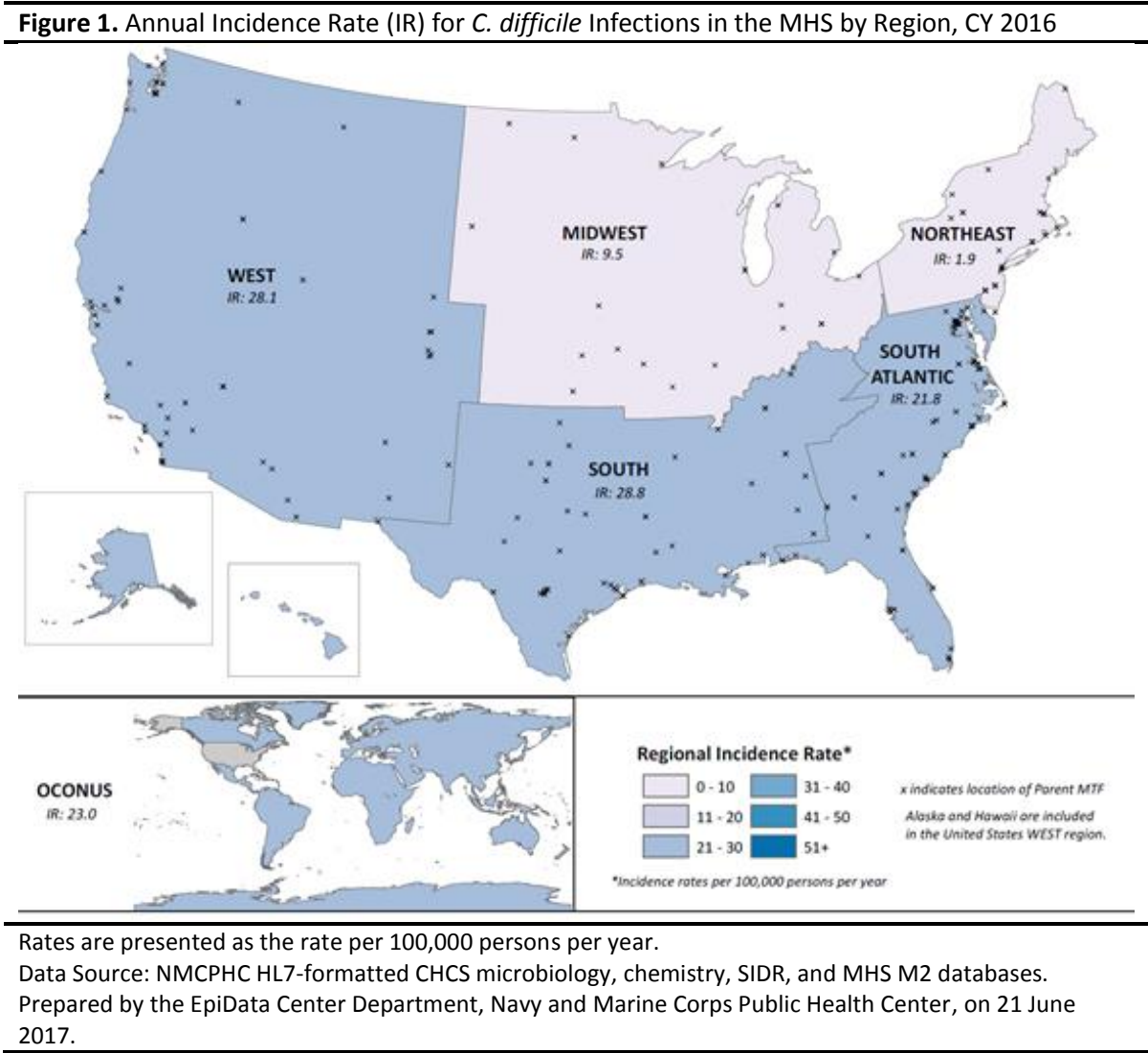
Demographic Distribution of *Clostridium difficile*

CDI was more likely to occur among family members (51.2%) and individuals aged 45 years and older (54.7%); CDI occurred almost equally by gender (Table 2). Approximately 10.5% (n = 207) of patients experiencing an incident CDI episode also experienced a recurrent CDI episode. The demographic distribution of patients with recurrent CDI was similar to patients who experienced an incident episode (data not shown).

Table 2. Demographic Characteristics of *Clostridium difficile* Infections in the MHS, CY 2016

	N = 1,969	
	Count	Percent
Gender		
Female	1,002	50.9
Male	967	49.1
Age Group (in Years)		
0-17	242	12.3
18-24	187	9.5
25-34	260	13.2
35-44	204	10.4
45-64	529	26.9
65+	547	27.8
Beneficiary Type		
Active Duty	345	17.5
Family Members	1,009	51.2
Retired	407	20.7
Other	208	10.6

The frequency is based on the demographic value of the index incident episode.
Data Source: NMCPHC HL7-formatted CHCS microbiology and chemistry databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

C. difficile Clinical Characteristics

Table 3 shows the most common comorbidities that are potential risk factors for CDI acquisition.[4] In 2016, diabetes, renal failure, and chronic pulmonary disease (COPD) were the three most frequent of the selected comorbidities among MHS CDI patients. Patients with these comorbidities represent a patient group within the MHS beneficiaries that may be especially vulnerable to worse health outcomes, such as recurrent CDI and increased risk of mortality.

Table 3. Selected Comorbid Medical Conditions among MHS Beneficiaries with CDI, 2016

Selected Comorbid Medical Conditions[a,b]	Count	Percent
Diabetes with or without chronic complications	330	16.8
Renal failure	269	13.7
Chronic pulmonary disease	245	12.4
Any cancer	181	9.2
Congestive heart failure	154	7.8
Liver disease	83	4.2

[a] The percent of each selected comorbidity among distinct CD incident infections.
[b] 1.8% of CDI patients had no MHS encounter data to evaluate comorbidity.
Data Source: NMCPHC HL7-formatted CHCS microbiology, chemistry, and SIDR databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Exposure Burden Metrics

Table 4 presents two different metrics for describing CDI rates for healthcare-associated exposures. The admission prevalence metric measures the magnitude of infection at the time of admission (importation of CDI into the healthcare system) or one year prior, and the overall prevalence metric measures the exposure of infection at any point during the admission or one year prior. In 2016, the total number of inpatient admissions for all MHS MTFs was 239,946. Among CDI patients, the overall prevalence rate was equal to or slightly higher than the admission prevalence rate in the MHS beneficiary population in all regions where region-specific rate calculation was applicable (Table 4). This finding suggests that the majority of CDI was imported into the hospital setting from the community, adding to the burden of CDI.

Table 4. *C. difficile* HAI Exposure Burden Metrics in the MHS, CY 2016

	Overall CDI Prevalence[a]		Admission CDI Prevalence[b]	
	Count	Rate[a]	Count	Rate[b]
Region				
OCONUS	19	1.1	17	1.0
US Midwest	25	2.6	25	2.6
US Northeast	1	– –	1	– –
US South	297	5.3	244	4.3
US South Atlantic	304	3.8	254	3.2
US West	423	5.7	340	4.6
Total	1,069	4.5	881	3.7

[a] Overall CDI prevalence included all individuals with CDI identified from a sample collected at any point during the admission, as well as samples that tested positive for infection in the prior calendar year.
[b] Admission prevalence included all individuals with CDI identified from samples collected up to and including the third day of admission, as well as samples that tested positive for infection in the prior calendar year.
[c] Rates are presented as the rate per 1,000 inpatient admissions per year. Rates are not calculated for counts less than or equal to ten.
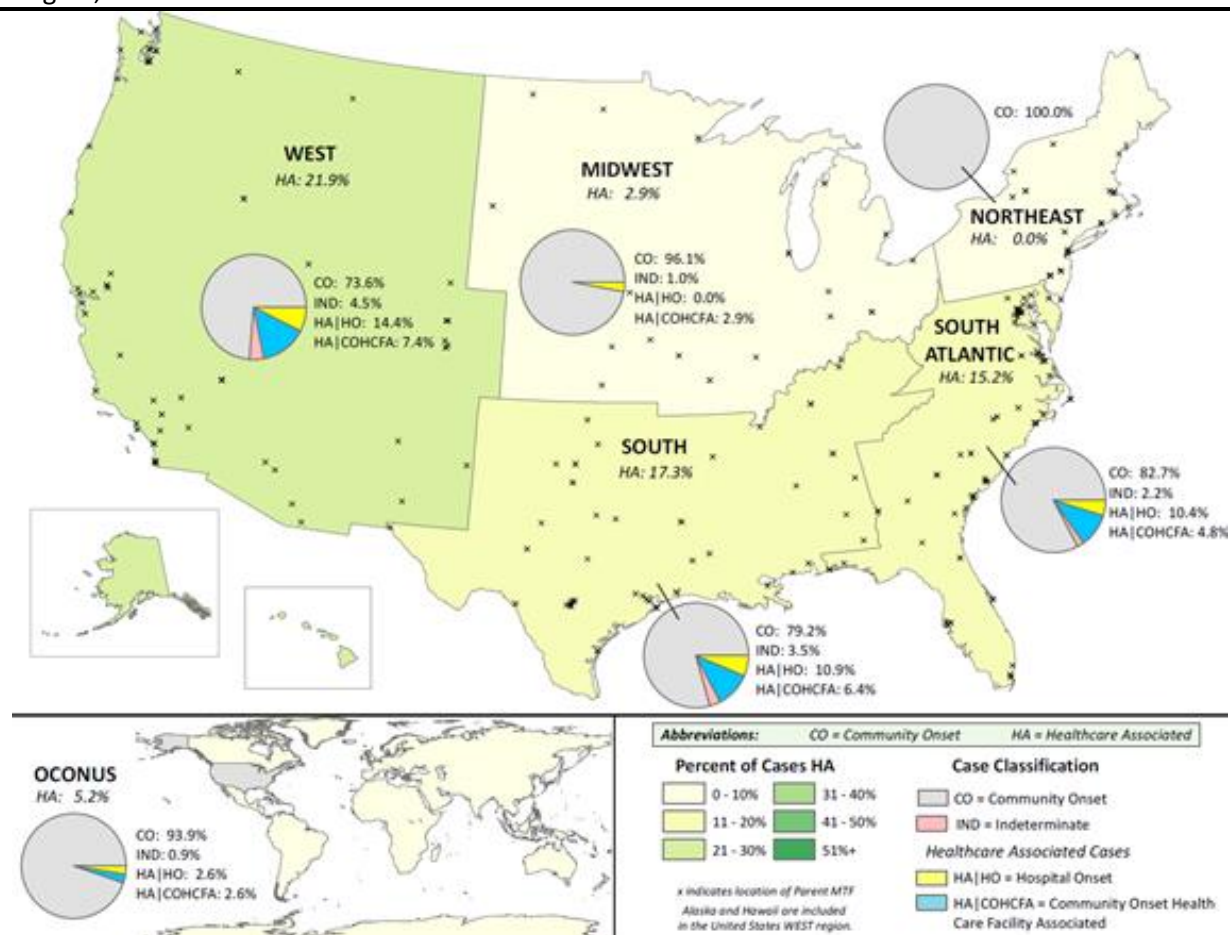Data Source: NMCPHC HL7-formatted CHCS microbiology and SIDR databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Regional Epidemiologic Infection Classifications

Overall, the majority of the 2,071 CDI incident episodes identified among MHS beneficiaries in CY 2016 were acquired in the community setting (CO) (80.3%) compared to the healthcare-associated (HA) setting (HO and CO-HCFA at 16.6%). Most CDI in the HA setting were HO CDI (10.8%) cases versus CO-HCFA CDI (5.8%) cases. The described trends were observed in both the United States (US) and OCONUS regions (Figure 2). The indeterminate category (IND) represents CDI that do not meet any exposure setting criteria.

Figure 2. Proportion of Healthcare- and Community-Associated *C. difficile* Infections in the MHS by Region, CY 2016

Data Source: NMCPHC HL7-formatted CHCS microbiology, SIDR, and MHS M2 databases.
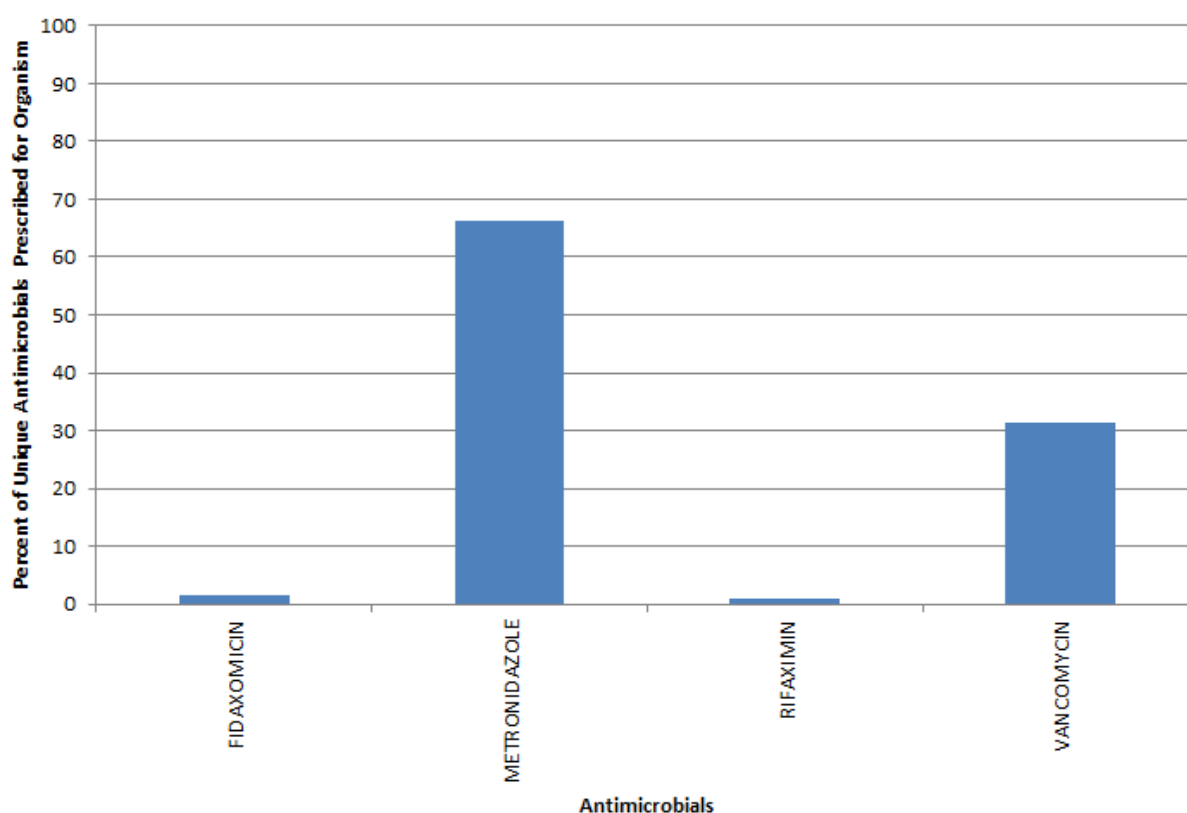Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Section B – Antimicrobial Use
Antimicrobial Consumption/Prescription Practices

Metronidazole was the most frequently prescribed medication for an initial CDI episode, representing 66.3% of CDI antibiotic treatment (Table 5).

Table 5. *C. difficile* Infection Prescription Practices in the MHS, CY 2016

The first occurrence of a unique antibiotic was counted per person per infection, regardless of administration route.
Data Source: NMCPHC HL7-formatted CHCS microbiology, chemistry, and pharmacy databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Use of antibiotics and gastric acid inhibitors is regarded as a risk factor for CDI. Table 6 shows that 67.3% of patients were prescribed an antibiotic within the 90 days prior to a CDI incident episode. The top three antibiotics prescribed were cephalosporins (generations 1-4), fluoroquinolones, and penicillin/penicillin beta-lactam inhibitors. Approximately 46.1% of CDI incident episodes had a gastric acid inhibitor prescribed 90 days prior to the incident event (PPIs [35.0%] and H2-receptor blockers [11.1%]).

Table 6. Selected Medication Use 90 Days Prior to CDI, MHS Beneficiaries, CY 2016

Any Antibiotic Class Prescribed[a]		
	Count	**Percent**
	1393	67.3
Selected Antibiotic Classes[b]		
Aminoglycosides	48	2.3
Carbapenems	114	5.5
Cephalosporins (generations 1-4)		
first generation	197	9.5
second generation	39	1.9
third generation	237	11.4
fourth generation	121	5.8
Clindamycin	303	14.6
Fluoroquinolones	561	27.1
Glycopeptides	276	13.3
Macrolides	112	5.4
Metronidazole	272	13.1
Nitrofuratoin	61	2.9
Other	32	1.5
Penicillins/penicillin beta-lactam inhibitors	630	30.4
Sulfonamides and/or trimethoprim	131	6.3
Tetracycline	66	3.2
Range	1-7	
Mean ± SD	2.3 ± 1.5	
Other Selected Medication Classes[c]		
Proton Pump Inhibitor	725	35.0
H2 Receptor Blocker	229	11.1

[a] The percent of antibiotics prescribed per class per CD incident episode (n = 1964) in the previous 90 days.
[b] The percent of each antibiotic class prescribed among CDI patients prescribed an antibiotic (n = 1329) in the previous 90 days.
[c] The percent of each gastric acid suppressant class prescribed per CD incident episode (n = 1964) in the previous 90 days.
Data Source: NMCPHC HL7-formatted CHCS microbiology, chemistry, and pharmacy databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Discussion

This report is a CY 2016 update to the CY 2015 *C. difficile* infection annual report for the MHS beneficiary population.[1] CDI incidence in the MHS population in both CY 2016 and CY 2015 showed normal variation when compared to the average annual incidence for CYs 2013-2015 and 2012-2014, respectively. Demographic and clinical characteristics were similar to trends reported in CY 2015. The burden of CDI continues to largely manifest in the community setting, among older age groups, and in patients with previous antibiotic and gastric-acid suppressant use. Patients with specific comorbidities considered risk factors for CDI, such as diabetes, renal failure, COPD, and cancers, represent a patient group within the MHS population that is especially vulnerable to worse health outcomes, such as recurrent CDI and increased risk of mortality. This group may especially benefit from prompt CDI identification and treatment.[4]

Interventions that reduce antibiotic exposure are the primary measures recommended to reduce CDI incidence and recurrence. These measures include limiting the use of unnecessary antibiotics, prescribing antibiotics that are lower risk for contributing to CDI, and using antibiotics for the shortest reasonable duration.[5] The MHS population can benefit from these interventions to decrease both CDI incidence and antibiotic selective pressure that may influence the development of multidrug-resistant organisms.

References

1. Neumann C, Chukwuma U. Annual surveillance summary: *Clostridium difficile* infections in the Military Health System (MHS), 2015. EpiData Center at the Navy and Marine Corps Public Health Center web site. http://www.med.navy.mil/sites/nmcphc/Documents/epi-data-center/Clostridium-difficile.pdf. Published March 2017. Accessed 21 June 2017.

2. EpiData Center at the Navy and Marine Corps Public Health Center. 2015 Surveillance Summaries: Bacterial Infections in the Military Health System (MHS). http://www.med.navy.mil/sites/nmcphc/epi-data-center/Pages/2015-surveillance-summaries.aspx. Published March 2017. Accessed 21 June 2017.

3. EpiData Center at the Navy and Marine Corps Public Health Center. 2016 Surveillance Summaries: Bacterial Infections in the Military Health System (MHS). http://www.med.navy.mil/sites/nmcphc/epi-data-center/Pages/2016-surveillance-summaries.aspx. Published June 2017. Accessed 30 June 2017.

4. Furuya-Kanamori L, Stone JC, Clark J, et al. Comorbidities, exposure to medications, and the risk of community-acquired *Clostridium difficile* infection: a systematic review and meta-analysis. *Infect Control Hosp Epidemiol*. 2015;36:132-41.

5. Association for Professionals in Infection Control and Epidemiology (APIC). Guide to Preventing *Clostridium difficile* infections. Washington, DC: APIC; 2013. http://apic.org/Resource_/EliminationGuideForm/59397fc6-3f90-43d1-9325-e8be75d86888/File/2013CDiffFinal.pdf. Published 2013. Accessed February 2017.

Appendix A: Acronym and Abbreviation List

Acronym/Abbreviation	Definition
CHCS	Composite Health Care System
CO	community-onset
CD	*Clostridium difficile*
CDI	*Clostridium difficile* infection
CO-HCFA	community-onset, healthcare facility associated
COPD	chronic obstructive pulmonary disease
CY	calendar year
EDC	EpiData Center Department
HA	healthcare-associated
HL7	Health Level 7
H-2	histamine-2
HO	hospital-onset
IR	incidence rate
M2	MHS Data Mart
MHS	Military Health System
MTF	military treatment facility
NMCPHC	Navy and Marine Corps Public Health Center
OCONUS	outside of the continental United States
PPIs	proton pump inhibitors
SD	standard deviation
US	United States